

support prior to step (d), wherein the second ion exchange precurs[e]or includes an ion exchange terminus blocked by a second protecting group.

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90. (Amended) The matrix of claim 89, wherein the method further comprises a step of removing the second protecting group from the second ion exchange precursor, thereby forming a second ion exchange ligand.

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93. (Amended) The method of claim 90, wherein relative proportions of a plurality of the first ion exchange residue and a plurality of the second ion exchange residue covalently attached to the solid phase are designed to control the charge ratio on the solid support surface, thereby controlling the binding affinity of the matrix for [(capacity remains more a property of the available particle surface) of the solid support to bind to the] a target nucleic acid material.

Please cancel claims 12, 22-85, and 99-100 without prejudice.

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Please add the following new claims:

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101. (New) The matrix of claim 1, wherein the plurality of ion exchange ligands covalently attached to the solid support has a density of at least about 25 μmol per gram dry weight of the matrix and no greater than about 500 μmol per gram dry weight of the matrix.

102. (New) The method of claim 90, wherein the plurality of first ion exchange ligands and the plurality of second ion exchange ligands covalently attached to the solid support have a density of at least about 25 μmol per gram dry weight of the matrix and no greater than about 500 μmol per gram dry weight of the matrix.

III. REMARKS

A. Amendments to Specification

The paragraph entitled CROSS-REFERENCE TO RELATED APPLICATIONS, on page 1 of the Specification, has been amended to indicate that the present application is a divisional of U.S. Application Number 09/312,172, filed May 14, 1999.

The brief descriptions of Figures 1-3 added to the BRIEF DESCRIPTION OF THE DRAWINGS section of the application, on page 11, are all supported by detailed descriptions of each drawing, beginning on page 21, line 16 of the Specification.

Figure 4 was referred to as "Figure 1" on page 11 and on page 41 of the specification of the application, as filed. Applicants submit that Figure 4 is the same figure identified as "Figure 1", therein. Both the general description on page 11 and the detailed description on page 41 clearly refer to a photograph, and not an illustration of a synthesis reaction. Figure 4 is the only one of the drawings submitted with the application which depicts a photograph.

The amendments to lines 7 and 8 of page 23 are introduced herein to correct a typographical error.

The amendments to line 19 of page 39 are introduced herein to insert a reference to the identifiers for the two nucleic acid sequences set forth therein, now identified in the attached Sequence Listing as SEQ ID NO:1 and SEQ ID NO:2, respectfully.

The amendments to page 41 to substitute "Figure 4" for "Figure 1" are made to correct an inadvertent error. Applicants respectfully submit that the accompanying text makes it clear that the figure described therein is a photograph of an electrophoresis gel. (See, e.g. p. 41, lines 9-13). Figure 4 is the only figure submitted with the patent application which is a reproduction of a photograph of any such gel. All the other figures are reaction diagrams.

Lines 23 and 25 of page 19 have been amended to indicate that the patent application referenced therein is U.S. Application Number 09/312,139, filed May 14, 1999, the same date as the filing date of the parent of the present application (i.e., U.S. Application Number 09/312,172). The application number of that application was, naturally, unavailable at the time the parent application was filed.

The present application is a divisional of U.S. Application Number 09/312,172, which was originally filed without a Sequence Listing. However, a Sequence Listing was filed by Applicants in that case on August 12, 1999, in response to a Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, mailed June 4, 1999. The only two sequences in the Sequence Listing were disclosed in the Specification of that application. The Sequence Listing filed in prosecution of Application Number

09/312,172 has been incorporated by reference into the present application, by filing of a Statement Under 37 C.F.R. §1.821(e), transmitted herewith.

Applicants respectfully submit that the amendments to the Specification introduced herein above, introduce no new matter into the application.

B. Amendments to the Claims and Claim Status

Claims 1-11, 13-21, 86-98, and 101-102 remain pending in the present application, after cancellation of claims 12, 22-85 and 99-100 and addition of new claims 101-102, as described above.

Applicants respectfully submit that no new matter has been added.

Claim 1 has been amended to remove the term "first" when used to refer to the "ion-exchange ligand" component of the pH dependent ion exchange matrix of the claim, as no "second" such ligand is referenced in the claim or in claims which depend therefrom. By making this amendment, however, Applicants do not intend to be limited to a pH dependent ion exchange matrix with only the one type of ligand set forth in claim 1.

Claim 1 has also been amended to state that the "acidic moiety" of the spacer component of the ion exchange ligand is a carboxyl residue. Basis for this amendment can be found on page 17, line 2. Claim 12, which defined the acidic moiety, as a member of a certain Markush group, has been canceled in view of the amendment to claim 1, above.

Claim 86 has been amended to incorporate most of the elements of claim 88 into claim 86. Specifically, step (b) of the method of claim 86 has been amended to indicate that a first ion exchange ligand precursor is provided. Claim 86 has also been amended to indicate that the spacer component of the first ion exchange ligand precursor includes an acidic substituent that is a carboxyl residue protected by a first protecting group. Step (d), a step of deprotecting the carboxyl residue by removing the first protecting group, thereby forming a first ion exchange ligand, has been added to claim 86. Applicants amend the language of claim 86, herein, to more clearly describe what they consider to be the subject invention.

Claim 88 has been amended to remove all elements expressly incorporated into claim 86, such that the amended claim specifies that the first protecting group is a methyl group.

Claim 89 has been amended to specify that the attachment of a second ligand precursor to the solid support occurs prior to deprotection, step (d) of claim 86. Basis for this amendment can also be found in the Specification on page 22, lines 20-23. Claim 89 has also been amended to correct a typographic error, changing "precursor" to --precursor--.

Claim 90 has been amended to clarify the language of the claim, referring to the process described therein as deprotecting, to be consistent with the language of step (d) of claim 86, after amendment.

Claim 93 has also been amended to clarify the language of the claim.

Finally, new claim 101 has been added, directed to the matrix of claim 1, wherein the density of the ligands in the matrix is at least about $25\mu\text{mol}$ per gram of dry weight of the matrix and no greater than $500\mu\text{mol}$ per gram of dry weight of the matrix. New claim 102 has been added, directed to the same range of ligand density in matrices produced according to the method of claim 86. Basis for both new claims can be found on page 19, lines 1-4, of the Specification.

Applicants respectfully submit that none of the amendments to the claims made herein above add any new matter to the application, filed herewith.

IV. SUMMARY

The Applicants respectfully submit that claims 1-11, 13-21 and 86-98, after amendment as described above and new claims 101-102 are in condition for allowance. Therefore, Applicants respectfully request an early notice of allowance. The Examiner is invited to contact the undersigned at the number indicated below with comments or questions about the application.

Respectfully submitted,

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